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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,834	02/16/2006	Jonathan Michael Blackburn	27353-513-US1	8870

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EXAMINER	
TSAY, MARSHA M	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/532,834	BLACKBURN ET AL.	
	Examiner	Art Unit	
	Marsha M. Tsay	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-42,44-77,79 and 80* is/are pending in the application.

4a) Of the above claim(s) *45-70 and 72-77* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-42,44,71,79 and 80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/28/09, 05/08/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 26, 2009 has been entered.

Applicants' arguments have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn.

Claims 1-39, 43, 78, 81 are canceled. Claims 45-70, 72-77 are withdrawn. Claims 40-42, 44, 71, 79-80 are currently under examination.

Priority: Applicants' request for priority to UK 0224872.2, filed October 25, 2002, is acknowledged.

Objections and Rejections

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 40-42, 44, 71, 79-80 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 40 and 71 recite a surface derivatized with antibiotic. It is unclear how what is meant by "antibiotic derived surface" (i.e., how is the surface derived with antibiotic). Further clarification is requested.

Claim 40 recites the limitation "said immobilized antibiotic" in the claim. There is insufficient antecedent basis for this limitation in the claim. Claim 40 recites providing a cellular lysate comprising a protein fused to a ble marker protein. It is unclear if the ble fusion protein is recombinant or if the lysate comprises the protein and then the ble is fused to the protein. Further clarification is requested. Claim 40 also recites detecting protein folding. It is unclear how protein folding can be detected by binding of the ble fusion protein to the immobilized antibiotic. It is noted that the ble marker will bind to the immobilized antibiotic but it is unclear how proper protein folding can be detected and/or assessed. Further clarification is requested.

Claim 44, line 2, recites expression product of a Sh ble, Tn 5 ble or Sa ble gene. The term "gene" should be used to identify Sh ble and Tn 5 ble, as well, since as currently written it is not clear if "Sh ble" or "Tn 5 ble" are also genes.

Claim 71 recites immobilizing the ble fusion protein on a surface derivatized with antibiotic from the bleomycin family and optionally releasing it therefrom. It is unclear how claim 71 distinguishes over claim 40 since claim 40 already recites binding and immobilization between antibiotic and the ble fusion protein. Therefore, the only additional limitation appears to be "optionally releasing it" (the ble fusion protein) therefrom, which is also confusing since it is unclear how the ble fusion protein is to be released from the antibiotic.

Claim 80 recites the ble fusion protein is detected by labeling antibiotic with a marker and detecting binding of the ble fusion protein to said marker. It is unclear why the ble fusion

protein would bind to the marker when it is believed that said ble fusion protein should bind to the antibiotic. Further, since claim 80 does not recite a specific marker, it is unclear if the antibiotic labeled with any marker would allow for proper binding to said ble fusion protein. Further clarification is requested.

Claims 41-42, 79 are included in this rejection because they are dependent on the above claims and fail to cure its defect.

In their remarks, Applicants did not address the previous 112, second paragraph, regarding "derivatized." Therefore, claims 40 and 71 remain rejected under 35 U.S.C. 112, second paragraph, indefiniteness, over the term "derivatized."

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 40-42, 44, 71, 79 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thinakaran (US 20030022151; IDS 05.28.09) in view of Takagi et al. (US 4610962). Thinakaran discloses a method for screening zeocin resistance in cells expressing a PS1 chimeric polypeptide (p. 21-22 [0248-0252]). A PS1 chimeric polypeptide comprises presenilin fused to a YFP (yellow fluorescent protein) and Sh ble (a ble marker protein) (p. 19 [0221]). Thinkaran further disclose that the antibiotic resistance gene (Sh ble) confers antibiotic resistance by stoichiometrically binding to an antibiotic (abstract). The antibiotic screening can be used to

detect changes in the levels of unstable chimeric proteins (abstract). Thinkaran discloses assays that measure binding of a molecule to said chimeric protein such that binding of a molecule to the chimeric protein may stabilize the protein (p. 9 [0105]). Thinkaran discloses various types of assays wherein said molecule can be bound to a surface or said protein can be bound to a surface; however, Thinkaran does not explicitly teach zeocin is immobilized onto a surface.

Takagi et al. (US 4610962) disclose carriers for immobilizing physiologically active substances (abstract). Takagi et al. also disclose that the immobilized carriers can be used in assays for detecting proteins (col. 7 lines 8-28). Takagi et al. disclose antibiotics, including bleomycin, are substances that can be immobilized onto the surface of the carriers (col. 2-3 lines 52-5).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Thinakaran et al. by immobilizing zeocin onto a surface as suggested by Takagi et al. for screening and/or assessing the binding of a chimeric protein comprising a fluorescent marker and a Sh ble protein marker (claims 40-42, 44, 71, 79). It would be reasonable for one of ordinary skill to know that screening assays can be modified such that either the molecule or protein is bound to the surface since regardless of which compound is immobilized, the binding reaction will still be detected and able to be quantified.

Regarding the instant limitation of detecting a protein expression and folding, it should be noted that the correct conformation and/or folding of the Sh ble-YFP fusion protein would naturally occur since Thinkaran discloses that the antibiotic (i.e. zeocin) binds to said protein. While the method of Thinkaran et al. in view of Takagi et al. may not explicitly disclose detecting protein expression and folding, the active steps of the instant invention are within the

scope of the method of Thinkaran et al. in view of Takagi et al.; therefore, even if the active steps of the instant invention are used for a different purpose does not alter the conclusion that its use in the prior art would be prima facie obvious from the purpose disclosed in the references. See also In re Lintner, 458 F.2d 1013, 1018, 173 USPQ 560, 562 (CCPA 1972). MPEP 2100.

It would also be reasonable for one of ordinary skill to know that said chimeric protein can be purified from the cells after expression since these skills and techniques are routine in the art and readily used in screening assays for proteins and molecules (Thinakaran p. 17 [0207]; claim 40, 71).

While Takagi et al. do not disclose detection by mass spectrometry, Applicants are again reminded that mass spectrometry is a method known in the art that can be used to quantify proteins; therefore, it would be reasonable for one of ordinary skill to know that any suitable and/or appropriate protein detection method can be used to assess protein binding to a molecule, i.e. antibiotic (claim 79).

Claim 80 is rejected under 35 U.S.C. 103(a) as being unpatentable over Thinakaran (US 20030022151) in view of Takagi et al. (US 4610962) in view of Calmels et al. (1993 Molecular Pharmacology 44: 1135-1141; previously cited). The teachings of Thinakaran et al. in view of Takagi et al. are outlined above. Thinakaran et al. in view of Takagi et al. do not teach a labeled antibiotic.

Calmels et al. disclose a fluorescently labeled antibiotic and that the protein product of the Sh ble gene binds to an antibiotic (bleomycin) with 1:1 stoichiometry (p. 1135).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Thinakaran et al. in view of Takagi et al. by substituting the fluorescently labeled antibiotic of Calmels et al. for the unlabeled antibiotic of Thinakaran et al. in view of Takagi et al. (claim 80). The motivation to do so is due to one of ordinary skill in the art's desire to generate a stronger visualization signal upon the protein binding to the antibiotic.

Applicants' remarks have been considered and the previous 103(a) rejection has been withdrawn. However, the newly cited references are believed to be relevant art under 103(a) for the reasons noted above.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is (571)272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Maryam Monshipouri/

Primary Examiner, Art Unit 1656

June 17, 2009